

CLAIMS

1. A pharmaceutical composition comprising:
- a therapeutically effective amount of a first compound, said first compound being an estrogen agonist/antagonist; and
 - a therapeutically effective amount of a second compound, said second compound being a prostaglandin or a prostaglandin agonist/antagonist.
2. A pharmaceutical composition as recited in claim 1 additionally comprising a pharmaceutical carrier.
3. A pharmaceutical composition as recited in claim 2 wherein the estrogen agonist/antagonist is droloxifene, raloxifene, tamoxifen, 4-hydroxy-tamoxifen,
- 10 Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol;
- (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol;
- 15 Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol;
- Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;
- 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-
- 20 tetrahydroisoquinoline;
- Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol; or
- 1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline.
4. A pharmaceutical composition according to claim 3 wherein the second compound
- 25 is PGD₁, PGD₂, PGE₂, PGE₁, PGF₂, PGF_{2α} or 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(1H-tetrazol-5-yl)-hexyl]-cyclopentanone.
- X 5. A pharmaceutical composition as recited in claim 4 wherein the estrogen agonist/antagonist is droloxifene.
- 5 6. A pharmaceutical composition according to claim 5 wherein the second compound
- 30 is PGE₂.
- 6 7. A pharmaceutical composition according to claim 5 wherein the second compound is 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(2H-tetrazol-5-yl)-hexyl]-cyclopentanone.

- 7 8. A pharmaceutical composition according to claim ⁴ wherein the estrogen agonist/antagonist is

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

- 5 (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

- 10 Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydro-naphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

- 15 1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline.

9. A pharmaceutical composition according to claim ⁷ wherein the second compound is PGE₂.

- 9 10. A pharmaceutical composition according to claim ⁷ wherein the second compound is 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(2H-tetrazol-5-yl)-hexyl]-cyclopentanone.

- 20 11. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. a therapeutically effective amount of a first compound, said first compound being an estrogen agonist/antagonist; and

- 25 b. a therapeutically effective amount of a second compound, said second compound being a prostaglandin or a prostaglandin agonist/antagonist.

- 11 12. A method as recited in claim ¹⁰ wherein the estrogen agonist/antagonist is droloxifene, raloxifene, tamoxifen, 4-hydroxy-tamoxifen, idoxifene, centrachroman,

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

- 30 (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

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Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

5 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

12 1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline.
10 13. A method as recited in claim 12 wherein the second compound is PGD₁, PGD₂, PGE₂, PGE₁, PGF₂, PGF₂ α or 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(1H-tetrazol-5-yl)-hexyl]-cyclopentanone.

13 14. A method as recited in claim 12 wherein the estrogen agonist/antagonist is droloxifene.

X 15 15. A method as recited in claim 14 wherein the second compound is PGE₂.

14 16. A method as recited in claim 14 wherein the second compound is 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(1H-tetrazol-5-yl)-hexyl]-cyclopentanone.

15 17. A method as recited in claim 14 wherein the condition which presents with low bone mass is osteoporosis.

20 16 18. A method as recited in claim 15 wherein the estrogen agonist/antagonist is

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

25 Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

30 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline.

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19. A method as recited in claim 18 wherein the second compound is PGE₂.
- 18
20. A method as recited in claim 18 wherein the second compound is 3S-(3-Hydroxy-4-phenyl-butyl)-2R-[6-(1H-tetrazol-5-yl)-hexyl]-cyclopentanone.
- 19
21. A method as recited in claim 18 wherein the condition which presents with low bone mass is osteoporosis.
- 20
22. A method as recited in claim 14 wherein the first compound and the second compounds are administered substantially simultaneously.
- 21
23. A method as recited in claim 14 wherein the second compound is administered for a period of from about three months to about three years.
- 10 22
24. A method as recited in claim 23 followed by administration of the first compound for a period of from about three months to about three years without the administration of the second compound during the period of from about three months to about three years.
- 23
25. A method as recited in claim 23 followed by administration of the first compound for a period greater than about three years without the administration of the second compound during the greater than about three year period.
- 24
26. A method as recited in claim 18 wherein the first compound and the second compounds are administered substantially simultaneously.
- 25
27. A method as recited in claim 18 wherein the second compound is administered for a period of from about three months to about three years.
- 20 26
28. A method as recited in claim 27 followed by administration of the first compound for a period of from about three months to about three years without the administration of the second compound during the period of from about three months to about three years.
- 25
29. A method as recited in claim 27 followed by administration of the first compound for a period greater than about three years without the administration of the second compound during the greater than about three year period.
- 28
30. A method for treating mammals which present with low bone mass comprising administering to a mammal having a condition which presents with low bone mass the pharmaceutical composition of claim 1.
- 30
31. A pharmaceutical composition comprising
a. an amount of a first compound, said first compound being an estrogen agonist/antagonist; and

b. an amount of a second compound, said second compound being a prostaglandin or a prostaglandin agonist/antagonist

wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

22. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. an amount of a first compound, said first compound being an estrogen agonist/antagonist; and

b. an amount of a second compound, said second compound being a prostaglandin or a prostaglandin agonist/antagonist

wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

29. 23. A kit containing a treatment for a condition which presents with low bone mass comprising:

a. a therapeutically effective amount of an estrogen agonist/antagonist and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of a prostaglandin or a prostaglandin agonist/antagonist and a pharmaceutically acceptable carrier in a second unit dosage form; and

c. container means for containing said first and second dosage forms.

30. 24. A pharmaceutical composition comprising:

a. a therapeutically effective amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

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b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl]carbonyl]-2-(phenylmethoxy)ethyl]-2-amino-2-methylpropanamide:MK-677.

5 ³¹35. A pharmaceutical composition as recited in claim ³⁰34 additionally comprising a pharmaceutical carrier.

36. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

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10 a. a therapeutically effective amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl]carbonyl]-2-(phenylmethoxy)ethyl]-2-amino-2-methylpropanamide:MK-677.

15 ³²37. A method as recited in claim ³²36 wherein the condition which presents with low bone mass is osteoporosis.

³⁴38. A method as recited in claim ³²36 wherein the first compound and the second compounds are administered substantially simultaneously.

20 ³⁵39. A method as recited in claim ³²36 wherein the second compound is administered for a period of from about three months to about three years.

³⁶40. A method as recited in claim ³⁵39 followed by administration of the first compound for a period of from about three months to about three years without the administration of the second compound during the period of from about three months to about three

25 years.

³⁷41. A method as recited in claim ³⁵39 followed by administration of the first compound for a period greater than about three years without the administration of the second compound during the greater than about three year period.

³⁸42. A method for treating mammals which present with low bone mass comprising

30 administering to a mammal having a condition which presents with low bone mass the pharmaceutical composition of claim ³⁰34.

43. A pharmaceutical composition comprising

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a. an amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

b. an amount of a second compound, said second compound being sodium fluoride or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677

wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

44. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. an amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

b. an amount of a second compound, said second compound being sodium fluoride or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677

wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

45. A kit containing a treatment for a condition which presents with low bone mass comprising:

a. a therapeutically effective amount of droloxifene, raloxifene, tamoxifen or idoxifene and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of a sodium fluoride or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677 and a pharmaceutically acceptable carrier in a second unit dosage form; and

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c. container means for containing said first and second dosage forms.

~~46. A pharmaceutical composition comprising:~~

a. a therapeutically effective amount of a first compound, said first compound being

5 Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol;

(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
10 naphthalene-2-ol;

Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

15 Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol; or

~~1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;~~

and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, growth hormone or a growth hormone secretagogue.

41 ~~47~~. A pharmaceutical composition as recited in claim ~~46~~ additionally comprising a pharmaceutical carrier.

42 ~~48~~. A pharmaceutical composition as recited in claim ~~47~~ wherein the second
25 compound is sodium fluoride. 41

43 49. A pharmaceutical composition as recited in claim 47 wherein the second compound is a parathyroid hormone. 41

44 50. A pharmaceutical composition as recited in claim ⁴¹ 47 wherein the second compound is growth hormone.

30 51. A pharmaceutical composition as recited in claim 47 wherein the second compound is a growth hormone secretagogue.

52. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. a therapeutically effective amount of a first compound, said first compound
5 being

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

10 Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

15 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

and

20 b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, growth hormone or a growth hormone secretagogue.

46 53. A method as recited in claim 52 wherein the second compound is sodium fluoride.

47 54. A method as recited in claim 52 wherein the second compound is a parathyroid
25 hormone.

48 55. A method as recited in claim 52 wherein the second compound is growth hormone.

56. A method as recited in claim 52 wherein the second compound is a growth hormone secretagogue.

30 49 57. A method as recited in claim 52 wherein the condition which presents with low bone mass is osteoporosis.

50 58. A method as recited in claim 52 wherein the first compound and the second compound are administered substantially simultaneously.

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- 51 59. A method as recited in claim ⁴⁵52 wherein the second compound is administered for a period of from about three months to about three years.
- 52 60. A method as recited in claim ⁵¹59 followed by administration of the first compound for a period of from about three months to about three years without the administration of the second compound during the period of from about three months to about three years.
- 53 61. A method as recited in claim ⁵¹59 followed by administration of the first compound for a period greater than about three years without the administration of the second compound during the greater than about three year period.
- 10 54 62. A method for treating mammals which present with low bone mass comprising administering to a mammal having a condition which presents with low bone mass the pharmaceutical composition of claim ⁴⁰45.
63. A pharmaceutical composition comprising
- 15 a. an amount of a first compound, said first compound being
- Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;
- (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;
- Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
- 20 naphthalene-2-ol;
- Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;
- 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;
- 25 Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or
- 1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;
- b. an amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, growth hormone or a growth hormone secretagogues
- 30 wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than

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the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

64. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with
- 5 low bone mass

a. an amount of a first compound, said first compound being

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol;

(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
10 naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol;

Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-
tetrahydrohaphthalene;

15 1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-
tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol; or

1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

20 and

b. an amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, growth hormone or a growth hormone secretagogue

wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein

25 the combined effect of the amounts of the first and second compounds is greater than the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

65. A kit containing a treatment for a condition which presents with low bone mass
- 30 comprising:

a. a therapeutically effective amount of

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-
naphthalene-2-ol;

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(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

5 Cis-1-[6'-pyrrolidinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

10 Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of sodium fluoride, a parathyroid hormone, growth hormone or a growth hormone secretagogue and a pharmaceutically acceptable carrier in a second unit dosage form; and

c. container means for containing said first and second dosage forms.

56 ~~66~~. The pharmaceutical composition as recited in claim ³⁰~~34~~ wherein the first compound is droloxifene.

57 ~~67~~. The method as recited in claim ³²~~36~~ wherein the first compound is droloxifene.

20 58 ~~68~~. The method as recited in claim ³⁶~~40~~ wherein the first compound is droloxifene.

59 69. The method as recited in claim ³²~~41~~ wherein the first compound is droloxifene.

~~70~~ 70. The pharmaceutical composition as recited in claim ~~43~~ wherein the first compound is droloxifene.

~~71~~ 71. The method as recited in claim ³⁹~~44~~ wherein the first compound is droloxifene.

25 ~~72~~ 72. The kit as recited in claim ~~45~~ wherein the first compound is droloxifene.

~~73~~ 73. A pharmaceutical composition comprising:

a. a therapeutically effective amount of a first compound, said first compound being raloxifene, tamoxifen or idoxifene;

and

30 b. a therapeutically effective amount of a second compound, said second compound being a parathyroid hormone, growth hormone or a growth hormone secretagogue.

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74. A pharmaceutical composition as recited in claim 73 additionally comprising a pharmaceutical carrier.
- 63 75. A pharmaceutical composition as recited in claim 74 wherein the first compound is raloxifene.
- 64
5 76. A pharmaceutical a composition as recited in claim 74 wherein the second compound is a parathyroid hormone.
- 63
77. A pharmaceutical composition as recited in claim 74 wherein the second compound is growth hormone.
78. A pharmaceutical composition as recited in claim 74 wherein the second compound is a growth hormone secretagogue.
- 10 79. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass
- a. a therapeutically effective amount of a first compound, said first compound
- 15 being raloxifene, tamoxifen or idoxifene;
- and
- b. a therapeutically effective amount of a second compound, said second compound being a parathyroid hormone, growth hormone or a growth hormone secretagogue.
- 65
20 80. A method as recited in claim 79 wherein the first compound is raloxifene.
- 64
81. A method as recited in claim 79 wherein the second compound is a parathyroid hormone.
- 69
82. A method as recited in claim 79 wherein the second compound is growth hormone.
- 25 83. A method as recited in claim 79 wherein the second compound is a growth hormone secretagogue.
- 66
84. A method as recited in claim 79 wherein the condition which presents with low bone mass is osteoporosis.
- 67
85. A method as recited in claim 79 wherein the first compound and the second compound are administered substantially simultaneously.
- 68
30 86. A method as recited in claim 79 wherein the second compound is administered for a period of from about three months to about three years.

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68
69 87. A method as recited in claim 86 followed by administration of the first compound for a period of from about three months to about three years without the administration of the second compound during the period of from about three months to about three years.

68
10 88. A method as recited in claim 86 followed by administration of the first compound for a period greater than about three years without the administration of the second compound during the greater than about three year period.

71 89. A method for treating mammals which present with low bone mass comprising administering to a mammal having a condition which presents with low bone mass the pharmaceutical composition of claim 73.

90. A pharmaceutical composition comprising
a. an amount of a first compound, said first compound being raloxifene, tamoxifen or idoxifene; or

b. an amount of a second compound, said second compound being a parathyroid hormone, growth hormone or a growth hormone secretagogues

15 wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than
20 the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

91. A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

25 a. an amount of a first compound, said first compound being raloxifene, tamoxifen or idoxifene;
and

b. an amount of a second compound, said second compound being a parathyroid hormone, growth hormone or a growth hormone secretagogue

30 wherein the amount of the first compound alone and the amount of the second compound alone is insufficient to achieve the therapeutic effects of increase in bone formation and decrease in bone resorption if administered simultaneously and wherein the combined effect of the amounts of the first and second compounds is greater than

-70-

the sum of the therapeutic effects achievable with the individual amounts of the first and second compound, and a pharmaceutically acceptable diluent or carrier.

32. A kit containing a treatment for a condition which presents with low bone mass comprising:

- 5 a. a therapeutically effective amount of raloxifene, tamoxifen or idoxifene;
and a pharmaceutically acceptable carrier in a first unit dosage form;
- b. a therapeutically effective amount of a parathyroid hormone, growth hormone
or a growth hormone secretagogue and a pharmaceutically acceptable carrier in a
second unit dosage form; and
- 10 c. container means for containing said first and second dosage forms.

Sub B⁸

Add B⁹